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Q-MYOCARDIAL INFARCTION BASED ON UNDIFFERENTIATED CONNECTIVE TISSUE DYSPLASIA: FROM PHENOTYPE TO CLINIC - BIOCHEMICAL CHARACTERISTICS

Summary. *A comparative analysis of phenotypic stigmas undifferentiated connective tissue dysplasia (UCTS), biochemical indexes, and the nature of complications of myocardial infarction (MI) in 62 patients (31 - with UCTS syndrome and 31 - without UCTS) with first diagnosed Q- MI. Defined correlation between the number of phenotypic and visceral stigmas of UCTS and complications of Q- MI ($r=0,97$; $p<0,05$). Disorders of lipid metabolism were not determinative risk factor of MI in patients with UCTS syndrome and without anamnesis of coronary artery disease (CAD) in development of Q-MI. Current Q-MI based on UCTS compared with Q-MI without UCTS at all levels of gender-age conditions and necrosis localization was less favorable, that is why UCTS syndrome can be considered as an adverse prognostic factor in myocardial infarction.*
Key words: *myocardial infarction, undifferentiated connective tissue dysplasia, phenotype.*

Introduction

Cardiovascular diseases (CVD) is truly called epidemic of XX century. Over the years, they are the leading cause of mortality in most of the countries, including Ukraine, making 65.8% of total mortality. So, for the past 25 years outspread of CVD among Ukrainian population was tripled, and the mortality rate from them - 45% [Горбась, 2007]. Outspread of coronary artery diseases (CHD) in Ukraine among people of working age in 2011 was 9.6 thousand to 100 thousand people, the mortality rate due to destabilization of coronary artery disease - 678 to 100 thousand people. According to official statistics of Ministry of Public Health of Ukraine for 2011 there were registered 49978 cases of acute myocardial infarction (MI) in Ukraine [Хобзей, Сіренко, 2013]. Modern coronary ventricle graphic studies indicate a significant percentage (12%) of patients suffered from MI and constant coronary vessels [Бокерия, Бухарин, 1999], which may be connected, in particular, with undifferentiated connective tissue dysplasia (UCTD) [Бокерия, Бухарин, 1999 ; Клеменов, 2005; Лобанов, Давтян, 2006]. According to modern concepts, UCTD is development disorder of connective tissue (CT) in embryonic and postnatal periods resulting genetically modified process of synthesis of external cellular matrix, which leads to changes in homeostasis at the tissue, organ, and organism levels in a variety of morphological disorders, visceral and locomotor organs [Нечаева, Яковлев, 2008]. Such aspect in studding of clinical and laboratory characteristics of MI is important, as outspreading of connective tissue dysplasia (CTD) in the general population makes 35% and in ecologically unfavorable regions is up to 50%. Topical character of a problem of CTD is defined also by wide affection of persons of working age [Евсевьева, Алейник, 2008].

CTD characterized morphologically by changes in collagen, elastic fibrils, glycoproteins, proteoglycans and fibroblasts, which are based on genetic determined mutations, that code synthesis and spaced collagen organization, structural protein and protein- carbohydrate complexes, and gene mutations of enzymes and cofactors to them [Kucharz, 1992]. Some researchers, basing on revealing magnesium deficiency in different substrates (hair, red blood cells, saliva) in 46,6-72,0% of cases with CTD, accept pathogenic role of hypomagnesemia [Кадурина, Горбунова, 2009; Серов, Шехтер, 1981; Шиляев, Шальнова, 2003]. There aren't universal pathological disorders of connective tissue, which would have formed a particular phenotype. Every defect of single patient is unique, and widespread connective tissue in the body determines multiple organ injuries at CTD [Нечаева, Яковлев, 2008].

Under clinical point of view, the most important is cardiovascular findings of CTD, as they turn on compensatory mechanisms, which based on metabolic disorders at CTD leads to acute myocardial insufficiency [Нечаев, Яковлев, 2008; Gelb, 2006]. Last years, new

trend in study of genetic determined disorders of connective tissue is widespread over the scientific world [Нечаева, Яковлев, 2008]. According to Яковлев В.М. et al., because of molecular genetic studies of collagen structure are at initial stage, it is appropriate to distinguish a group of "undifferentiated connective tissue dysplasia" [Яковлев, Карпов, 2001]. The authors believe that the basis of UCTD diagnosis is internal and external phenotypic characteristics, and diagnostic difficulties associates with absence or poor knowledge of phenotypic characteristics and clinical reveals of UCTD. Based on above mentioned, there are studies that showed certain peculiarities and prognosis of internal organs diseases in patients with UCTD. There were identified features of pathology of cardiovascular system associated with UCTD [Евсевьева, Алейник, 2008; Нечаева, Яковлев, 2008]. Researched methods of UCTD diagnostic, in particular, revealing of biochemical markers of UCTD [Доценко, Герасименко, 2011; Осипенко, 2012; Осипенко, Солейко, 2012], indices of diastolic function of left ventricular at myocardial infarction and CTD [Евсевьева, Алейник, 2008], morphological reasoning of cardiovascular findings of UCTD [Доценко, Герасименко, 2011]. There are new prospects for metabolic treatment of cardiologic pathology based on UCTD [Осипенко, 2012]. But there is still a question of effect of UCTD to Q- MI, its clinical and laboratory characteristics in patients of different age and CAD anamnesis. Problem of UCTD can be considered of weak structure as no unified algorithmic solutions.

Purpose: to study and analyze the clinical characteristics and complications of Q-IM in patients with UCTD.

Materials and methods

The study involved 62 patients aged of 36 to 84 years old (average age 58,08±1,37 years old), who live in Vinnytsia and Vinnytsia region, with first diagnosed Q- MI, admitted to in-patient department on the first day of disease. They were supervised while their stay at in-patient department.

According to the number of phenotypic and visceral stigmas of USTD patients were divided into 2 groups.

The basic group included 31 patients with USTD syndrome (number of phenotypic and visceral stigmas of USTD was 6 or higher).

Comparison group consisted of 31 patients without the USTD syndrome (number of phenotypic and visceral stigmas of USTD was 5 or less).

Inclusion criterions were comorbidities nosologies affecting the clinical features, course and development of complications of Q- MI: arterial hypertension, obesity (Quetelet index > 30 kg/m2), diabetes mellitus, other severe comorbidities (COPD, malignancies). Patients with recurrent Q- MI were excluded from the study.

The majority of patients included in the study made males - 51 (82.26%).

Studied the following anthropometric characteristics by method of V.V.Bunaka (1939, 1941) in the modification of P.P.Shaparenka [Шапаренко, 1994]: body mass, body height, neck length, body length, lower extremity length, thorax length, head circumference, chest circumference. Joint hypermobility was estimated by the following tests: elbow and knee joints hyperextension, the thumb touching the forearm at bending the wrist, finger sets parallel to the forearm wrist at extending the wrist and metacarpal joint; dorsal extension of the foot more than 45°. If the patient had three of five pairs features showed above, it was registered as hypermobility of joints. Increased skin hyperextensibility was considered as existing in pulling off it for 2-3 cm in wrist area, forehead, over the external parts of the clavicles with no pain in the patient. Ocular symptoms of UCTD were evaluated anamnesticly, clinically, ophthalmometricly. Ear markers were detected while clinical examination.

All patients did a questionnaire using a specially designed original questionnaire survey based on phenotype map of M.J.Glesby in modification of A.I.Martynov et al. for the analysis of phenotypic markers of UCTD. The questionnaire included 54 positions of microanomalies. There were counted the number of phenotypic and visceral dysembryogenetic stigma at the end of survey. Revealing 6 or more positions of microanomalies lead to UCTD in patient.

Mathematical analysis of the results included the following methods: initial calculation of statistical indicators; to identify differences between groups by statistical grounds, establishment the connection between the variables using parametric (Pearson correlation) correlation analysis. Primary statistical analysis for quantitative indicators included calculation of the arithmetic mean (M), the error of arithmetic mean value (m). Difference between samples, divided by normal distribution law was estimated by Student t-test (t) for unbound measurements. Scale of significance ($p<0,05$) was taken as statistical confidence. Mathematical processing was performed on personal computer using standard statistical package STATISTICA 6,0.

Results. Discussion

First phase of this study found the history of coronary artery disease before development of Q-MI in patients of the basic group and the comparison one. We have found that the percentage of patients with coronary artery disease without CAD in anamnesis before development of Q-MI was significantly ($p<0.05$) lower in the basic group and made 41.94% against 64.52% in the comparison one. At the same time there was an opposite situation in patients with coronary artery disease of 10-15 years in anamnesis before development of Q-MI: percentage was 9.68% in patients with UCTD syndrome, but the comparison group has no patients with such long-term history of CAD. The average age of patients without CAD in anamnesis before development of Q-MI in the basic group was 55,62±2,88 years old, and patients without UCTD - 58,05±2,69 years old. The average age of patients of the basic group with CAD in anamnesis over 10 years was 53,33±3,93 years old.

Obtained results show that the length of CAD in anamnesis before development of Q-MI in patients with UCTD is longer

than in patients without UCTD.

After analyzing markers of UCTD obtained during somatometric examination and questioning of patients, according to a questionnaire created by us, it was found statistical confidence difference between average number of UCTD markers in patients of the basic group (8,03±0,38) and comparison group (4,42±0,13) ($p<0.05$). 2 patients of the basic group (6.45%) had 12 markers, 3 (9.68%) - 11 indicators, 1 patient had 10 indicators (3.23%), 9 markers was found in 6 persons (19.35%), 8 (25.81%) - 8 markers, 7 persons (22.58%) had 7 indicators of UCTD and 4 (12.90%) - 6 indicators.

The markers of UCTD were selected by topographic principle in patients of the basic group and the comparison group. Qualitative analysis of dysembryogenetic stigma by injury localization showed the following changes. All patients - 62 (100%) - had various microanomalies of connective tissues of hands and feet. Among patients with UCTD the second place of injury frequency took ocular stigma (radial and lacunar iris, blue sclera) and microanomalies of auricle (diagonal earlap fold, small lobe) - in 29 persons (93.55%); changes in the oral cavity (bite anomalies, tendency to premature caries, diastema) were found in 25 patients (80.65%). At the same time patients group without UCTD second place of injury frequency took anomalies of auricle (diagonal earlap fold) - 20 persons (64.52%), but ocular stigma (radial and lacunar iris, blue sclera) had much smaller number of patients - 9 (29.03%). Plus, under increasing number of UCTD stigma the incidence of the following microanomalies significantly increased also: anomalies of auricle, blue sclera, scoliosis, chest deformity, hematoma formation with slight damage, tendency to premature caries ($p<0.05$). By the number of affected system there were the next trends among patients of basic group: 6.45% of patients had a stigma in 3 systems, 25.81% - 4 systems, 38,71% - 5 systems, 25.81% - 6 systems, 3, 23% - all of 7 systems. No patient had phenotype and visceral stigma in two systems only. 9.68% of patients of comparison group had 2 affected systems, 45,16% - 3 systems, 35.18% - 4 systems and 9.68% - 5 systems. There were not found combinations of 6 and 7 affected systems in this patients group at all. According to received results the majority of combination of several affected systems with multiple dysembryogenetic stigma made ocular and auricle stigma among the patients of basic group.

The next step of this study was to analyze the nature of Q-MI early complications in basic group (Table 1). Established that the biggest percentage of complications accounted for arrhythmias and conduction, that was revealed in 29.03% of patients of basic group and 25.81% in comparison group. Postinfarction aneurysm (22.58%), interventricular septal rupture (3.23%), rupture of papillary muscles (3.23%), cardiogenic shock (3.23%) and Dreslera syndrome (3, 23%) were found among the patients of basic group. Patients without UCTD had none of these Q-MI complications. Using correlation analysis and Pearson's linear correlation coefficient

Table 1. Characteristic of early complications of Q-MI in basic group and comparison group (n=62).

Complications of Q-MI	Basic group (n=31),%	Comparison group (n=31),%
Arrhythmia and conduction disorders	29,03	25,81
Postinfarction aneurysm	22,58*	0
Interventricular septal rupture / papillary muscle rupture	6,45	0
Acute heart failure (Killip I, II, III)	16,13	9,68
Cardiogenic shock	3,23	0
Dressler's syndrome	3,23	0

Note: * - significant difference between basic group and comparison group ($p<0.05$).

Table 2. Biochemical indicators of patients of basic group and comparison group (n=62) (M±m).

Indicator	Basic group (n=31)	Comparison group (n=31)
Lipids, g/l	6,40±0,17	6,89±0,19
Cholesterol , mmol/l	4,9±0,11	5,01±0,11
β - lipoproteins, un	51,65±1,21	52,71±1,13
Triglycerides, mmol/l	1,53±0,05*	1,75±0,06
Alanine aminotransferase, mkol/(h / l)	0,488±0,029	0,508±0,034
Aspartate aminotransferase, mkol/(h/l)	0,441±0,026	0,463±0,033

Note: *- significant difference between basic group and comparison group ($p<0.05$).

there was found a strong direct bond between the number of phenotypic and visceral stigma of UCTD and early complications of Q-MI in patients of basic group ($r=0,97$; $p<0.05$).

Hereby, Q-MI based on UCTD is less favorable for the frequency and nature of early complications of MI compared with patients without UCTD.

During analyzing the results of laboratory studies of peripheral blood, we decided to highlight the level of the following indexes: WBC, ESR, lipids, cholesterol, β-lipoprotein, triglycerides.

Average WBC values in blood of patients of basic group were 8,83±0,66 x 10^9, but comparison group - 9,85±0,8 x 10^9. Leukocytosis was found in 29,03±8,15% of patients of basic group and 51,61±8,98% of comparison group. Average values of ESR in basic group were equal to 20,42±2,45 mm/h , and made 19,39±2,57 mm/h in comparison group of patients. Increased ESR was recorded in basic group and comparison group with frequency of 64,16±8,59% and 70,97±8,15% respectively.

Clinical analysis expressed nonspecific reaction to tissue necrosis of myocardium. At admission to the hospital, the number of patients with leukocytosis in basic group was less than one-third, but leukocytosis was recorded in more than a half of patients of comparison group. However, despite rather heterogeneous rates of indexes such as WBC and

ESR, statistically significant difference was not found (p>0,05).

Lipid metabolism test revealed the average indexes of lipids were within normal limits in both study groups (Table 2). However, the average indexes of cholesterol, β-lipoprotein and triglycerides had the standard indicators only in patients with UCTD syndrome and made 4,9±0,11 mmol/l , 51,65±1,21 units and 1,53±0.05 mmol/l, respectively. At the same time patients of comparison group had average indexes of cholesterol (5,01±0,11 mmol/l), β- lipoproteins (52,71±1,13 units) and triglycerides (1,75±0,06 mmol/l) higher than the standard ones.

Statistically significant difference between lipid abnormalities was found between the average level of triglycerides in patients of basic group - 1,53±0,05 mmol/l, and comparison group - 1,75±0,06 mmol/l (p<0.05). Hypercholesterolemia was diagnosed in 35,48±8,48% of patients of basic group and 51,61±8,98% - comparison group. Average cholesterol index in patients without coronary artery disease in anamnesis before development of Q-MI was significantly lower in basic group, and made 4.62 mmol/l vs. 5.03 mmol/l in comparison group (p<0.05). So, lipid metabolism disorder was not key risk factor for CAD and MI in patients with UCTD syndrome, who do not have experience of CAD before development of Q-MI in particular.

Hereby, the results of the study indicate that UCTD may affect the clinical course of MI: length of CAD in anamnesis before development of Q-MI, the number and nature of early complications of Q-MI, changes in lipid metabolism (average indexes of cholesterol, β -lipoproteins and triglycerides).

Conclusions and recommendations for further development

1. Length of CAD in anamnesis before development of Q-MI in patients with UTCD is longer than in patients without UTCD. Lipid metabolism disorder was not key risk factor for CAD and MI in patients with UCTD syndrome, who do not have experience of CAD before development of Q-MI in particular.

2. Correlation analysis revealed bond between number of phenotypic and visceral stigmas of UCTD and complications of Q- MI (r = 0,97; p < 0.05). Differences in the frequency of postinfarction aneurysm formation in patients with UCTD syndrome were the most significant.

3. Most of patients with UCTD had dysembryogenetic stigma such as radial lacunar iris and diagonal earlap fold; under increasing number of UCTD stigma significantly increased frequency of finding the following microanomalies: anomalies of auricle, blue sclera, scoliosis, chest deformity, hematoma formation with slight damage, tendency to premature caries (p<0.05). Flow of Q-MI based on UCTD compared with Q-MI without UCTD under all equal gender-age conditions and localization of necrosis is less favorable that is why UCTD syndrome can be considered as an unfavorable prognostic factor in myocardial infarction.

Revealing of phenotypic markers of UCTD and in-depth analysis of clinical and biochemical characteristics of Q- MI based on UCTD allows further improving treatment and quality of life of the patients, and is a prospective area for cardiac research.

Literature

Горбась І.М. Фактори ризику серцево-судинних захворювань: поширеність і контроль /І.М.Горбась // Здоров'я України.- 2007.- №21.- С.62-63.

Гострий коронарний синдром з елевацією сегмента ST (екстрена, первинна, вторинна (спеціалізована) медична допомога): Уніфікований клінічний протокол медичної допомоги / М.К.Хобзей, Ю.М.Сіренко, А.В.Вершигора [та ін.].- 2013.- Версія №8.- С.8.

Дисплазия соединительной ткани: основные клинические синдромы, формулировка диагноза, лечение /Г.И.Нечаева, В.М.Яковлев, В.П.Конев [и др.] //Лечащий врач.- 2008.- №2.- С.22-25.

Евсевьева М.Е. Ремоделирование миокарда у больных ИБС с учетом дисплазии соединительной ткани /М.Е-.Евсевьева, О.Н.Алейник, Е.А.Власянц //Матер. VII съезда кардиологов Южного федерального округа.- Ростов-на-Дону, 2008.- С.101-102.

Кадурина Т.И. Дисплазия соединительной ткани /Т.И.Кадурина, В.Н.Горбунова.- СПб.: ЭЛБИ, 2009.- 714с.

Клеменов А.В. Недифференцированные дисплазии соединительной ткани / А.В.Клеменов.- М.: Медицина, 2005.- 136с.

Лобанов М.Ю. Дисплазия соединительной ткани как фактор риска развития фибрилляции предсердий у больных ИБС /М.Ю.Лобанов, К.У.-Давтян, Э.В.Земцовский //Тезисы VII Всеросс. конф. "Современные возможности холтеровского мониторирования" //Вестник аритмологии.- Прил.- СПб.- 2006.- С.79-80.

Морфологічне обгрунтування серцево-судинних проявів дисплазії сполучної тканини /М.Я.Доценко, Л.В.Герасименко, С.С.Боєв [та ін.] //Укр. терапевт. журнал.- 2011.- №3.- С.122-125.

Осипенко І.П. Зміни альдостерону та кортизолу сироватки крові у пацієнтів з ідіопатичним пролабуванням мітрального клапану /І.П.Осипенко, О.В.Солєйко, Л.О.Крижанівська [та ін.] /Тези доп. V Нац. конгресу "Людина та ліки України".- 2012.- С.88.

Осипенко І.П. Колагеностимулююча дія комплексної терапії препаратами магнію та гліцином у чоловіків із ідіопатичним пролапсом мітрального клапану /І.П.Осипенко // Biomedical and Biosocial Anthropology.- 2012.- №19.- С.171-175.

Осипенко І.П. Особливості амінокислотного складу сироватки крові у пацієнтів із ідіопатичним пролапсом мітрального клапану /І.П.Осипенко //Вісник Вінницького нац. мед. унів.- 2012.- Т.16, №2.- С.358-361.

Серов В.В. Соединительная ткань (функциональная морфология и общая патология) /В.В.Серов, А.Б.Шехтер.- М.: Медицина, 1981.- 312с.

Хирургическое лечение больных ишемической болезнью сердца с поражением брахиоцефальных артерий /Л.А.-Бокерия, В.А.Бухарин, В.С.Работников [и др.].- М.: НЦССХ им. А.Н.Бакулева РАМН, 1999.- С.76-83.

Шапаренко П.Ф. Принцип пропорциональности в соматогенезе: Монография /Шапаренко П.Ф.- Винница: Центр НИТ ВМИ, 1994.- 225с.

Шиляев Р.Р. Дисплазия соединительной ткани и ее связь с патологией внутренних органов у детей и взрослых / Р.Р.Шиляев, С.Н.Шальнова //Вопр. совр. педиатрии.- 2003.- №5.- С.61-67.

Яковлев В.М. Нарушения ритма и проводимости при соединительноткан-

ной дисплазии сердца /В.М.Яковлев, Р.С.Карпов, Ю.Б.Белан.- Омск: Изд-во ОГМА, 2001.- 160с.

Gelb B. Marfan's syndrome and related disorders - more tightly connected than we thought /B.Gelb //New Engl. J. Med.- 2006.- Vol.355, №8.- P.841-844.

Kucharz E. The Collagens: Biochemistry and Pathophysiology /E.Kucharz.- New York.: SpingerVerlag, 1992.- 430p.

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Q-ІНФАРКТ МІОКАРДА НА ТЛІ НЕДИФЕРНЦІЙОВАНОЇ ДИСПЛАЗІЇ СПОЛУЧНОЇ ТКАНИНИ: ВІД ФЕНОТИПУ ДО КЛІНІКО-БІОХІМІЧНИХ ОСОБЛИВОСТЕЙ

Резюме. *Проведено порівняльний аналіз фенотипових стигм недиференційованої дисплазії сполучної тканини (НДСТ), біохімічних показників, та характеру ускладнень інфаркту міокарда (ІМ) у 62 пацієнтів (31 - із синдромом НДСТ та 31 - без НДСТ) із вперше встановленим Q-ІМ. Встановлений кореляційний зв'язок між числом фенотипових і вісцеральних стигм НДСТ та наявністю ускладнень Q-ІМ (r=0,97; p<0,05). Порушення ліпідного обміну не являлись вирішальним фактором ризику ІМ у пацієнтів з синдромом НДСТ і відсутнім стажем ішемічної хвороби серця (ІХС) до розвитку Q-ІМ. Перебіг Q-ІМ на тлі НДСТ порівняно з Q-ІМ без її наявності за всіх рівних гендерно-вікових умов та локалізації некрозу виявився менш сприятливим, тому синдром НДСТ можна розглядати як несприятливий прогностичний фактор при ІМ.*

Ключові слова: *інфаркт міокарда, недиференційована дисплазія сполучної тканини, фенотип.*

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Q-ИНФАРКТ МИОКАРДА НА ФОНЕ НЕДИФФЕРЕНЦИРОВАННОЙ ДИСПЛАЗИИ СОЕДИНИТЕЛЬНОЙ ТКАНИ: ОТ ФЕНОТИПА ДО КЛИНИКО-БИОХИМИЧЕСКИХ ОСОБЕННОСТЕЙ

Резюме. *Проведен сравнительный анализ фенотипических стигм недифференцированной дисплазии соединительной ткани (НДСТ), биохимических показателей и характера осложнений инфаркта миокарда (ИМ) у 62 пациентов (31 - с наличием синдрома НДСТ и 31 - без НДСТ) с впервые установленным Q-ИМ. Установлено корреляционную связь между числом фенотипических и висцеральных стигм НДСТ и наличием осложнений Q-ИМ (r=0,97, p<0,05). Нарушения липидного обмена не являлись решающим фактором риска ИМ у пациентов с синдромом НДСТ и отсутствующим стажем ишемической болезни сердца (ИБС) до развития Q-ІМ. Течение Q-ИМ на фоне НДСТ по сравнению с Q-ИМ без ее наличия при всех равных гендерно-возрастных условиях и локализации некроза оказалось менее благоприятным, поэтому синдром НДСТ можно рассматривать как неблагоприятный прогностический фактор при ИМ.*

Ключевые слова: *инфаркт миокарда, недифференцированная дисплазия соединительной ткани, фенотип.*

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